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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/762,128	01/20/2004	Nathalie B. Scholler	920010.702C1	4107

500 7590 05/31/2007

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EXAMINER	
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ART UNIT	PAPER NUMBER
1632	

MAIL DATE	DELIVERY MODE
05/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/762,128	SCHOLLER ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *2,4,6 and 8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5 and 7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 January 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/26/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' election without traverse of Group I, Claims 1, 3, 5, and 7, in the response filed March 5, 2007 is acknowledged. The elected invention is drawn to a vaccine comprising one or more recombinant expression constructs (i.e., DNA vaccine compositions).

The restriction requirement is still deemed proper and is therefore made FINAL.

Claims 1-8 remain pending in the instant application.

Claims 2, 4, 6, and 8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on March 5, 2007.

Accordingly, Claims 1, 3, 5, and 7 are examined herein.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 3, 5, and 7 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-4 of U.S. Patent No. 6,734,172. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the earlier-filed application are directed to a species that falls within the presently claimed genus. Thus, the claims of the patent anticipate the present claims (anticipation analysis).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5, and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vaccine composition for eliciting or enhancing the titer of antibodies for Her2/neu protein, wherein the vaccine composition comprises one or more individual expression constructs encoding Her2/neu, CD86/B7.2, and 4-1BB ligand, does not reasonably provide enablement for other vaccine compositions for eliciting or enhancing the titer of antibodies for any cell surface receptor antigen, wherein the vaccine composition comprises one or more recombinant expression constructs encoding any cell surface receptor antigen plus any two immune response altering molecules,

consisting of any accessory cell agent and any T cell agent, as set forth in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, are set forth in *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988). These factors include: (1) the nature of the invention, (2) the state of the prior art, (3) the relative level of skill of those in the art, (4) the predictability of the art, (5) the breadth of the claims, (6) the amount of direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary (MPEP 2164.01(a)).

Giving due consideration to all the Wands factors, with the most relevant factors discussed hereinbelow, it is concluded that the specification fails to provide an enabling disclosure for the full scope of the claims, for the reasons that follow.

Nature of the invention and scope of the claims. The claims are drawn to a vaccine for eliciting or enhancing the titer of antibodies specific for a cell surface receptor antigen, comprising one or more recombinant expression constructs comprising at least one promoter operably linked to cassettes encoding a cell surface receptor antigen (SRA), a first immune response altering molecule (IRAM), and a second IRAM, wherein said first and second IRAMs are different from each other and are selected from the group consisting of an accessory cell agent and a T cell agent. Claim 1 is directed to a vaccine comprising a single recombinant expression construct encoding all three components. Claim 3 is directed to a vaccine comprising two recombinant expression constructs, one encoding the SRA and first IRAM and one encoding the second IRAM. Claim 5 is directed to a vaccine comprising three recombinant expression constructs, each encoding one component. Claim 7 is directed to a vaccine comprising two recombinant expression constructs, with one encoding the SRA and one encoding the two IRAMs. The

claims cover vaccines for cancer immunotherapy or any other purpose. The term "vaccine" denotes an intended use for producing a protective or prophylactic immune response.

Amount of direction or guidance presented and the presence or absence of working examples. The specification describes the construction of four recombinant expression constructs based on the plasmid pLNCX. The four plasmids generated were designated pLNCX-4-1BBlig, pLNCX-B7.1, pLNCX-B7.2, and pLNCX-Rat-Neu and the CMV promoter was used to drive expression of each component. The plasmid pLNCX-4-1BBlig contains a gene encoding the murine 4-1BB ligand. pLNCX-B7.1 contains a cDNA sequence encoding murine B7.1. pLNCX-B7.2 contains a cDNA encoding murine B7.2. pLNCX-Rat-Neu contains a gene encoding the rat Neu surface receptor antigen. FVB/N-TgN(MMTVneu) were used for immunization studies. The mice are transgenic for the rat Neu2 transgene under the control of a mouse mammary tumor virus promoter (MMTV LTR) and develop spontaneous mammary tumors with advanced age. Seven groups of mice were vaccinated with the plasmids by intradermal injection, as follows: pLNCX (Group 1, control), pLNCX-Rat-Neu (Group 2), pLNCX-Rat-Neu + pLNCX-B7.1 (Group 3), pLNCX-Rat-Neu + pLNCX-B7.2 (Group 4), pLNCX-Rat-Neu + pLNCX-4-1BBlig (Group 5), pLNCX-Rat-Neu + pLNCX-B7.1 + pLNCX-4-1BBlig (Group 6), pLNCX-Rat-Neu + pLNCX-B7.2 + pLNCX-4-1BBlig (Group 7). A booster immunization was injected 15 days later along with a dorsal subcutaneous challenge with mammary tumor cells from untreated transgenic mice. Neu-specific antibodies were detected in the sera of immunized mice by antigen-capture ELISA. Groups 3, 5, 6, and 7 all exhibited significantly elevated levels of anti-Neu antibodies compared to the control and Group 2 mice immunized with pLNCX-Rat-Neu alone. Tumor surface area increased as a function of time in mice of all treatment groups. An impaired tumor growth rate and decreased tumor burden were apparent in Group 7 mice. Group 4 mice, immunized with pLNCX-Rat-Neu + pLNCX-B7.2, exhibited an **increase** in tumor size and an increase in tumor growth rate.

The specification contemplates that the claimed vaccine may include expression constructs encoding a huge variety of immune response altering molecules (IRAM) (pages 11-16) in combination with any cell surface receptor antigen (pages 8-10). However, only the combinations discussed above are described. The specification fails to describe or provide specific guidance for any other combination that would elicit antibodies specific for a cell surface receptor antigen. While the specification contemplates a wide variety of agents that may be used as IRAM and a wide variety of agents that may be used as the SRA, the specification provides no guidance at all for specific combinations of two IRAM with one cell surface receptor antigen that would elicit an antibody response, other than the two combinations discussed above for producing Neu-specific antibodies, where a gene encoding either B7.1 or B7.2 is used in combination with genes encoding 4-1BB ligand and rat Neu. The specification provides **no** specific guidance for other combinations. Thus, the specification fails to provide an enabling disclosure for other combinations that would elicit SRA-specific antibodies.

Beyond the specific vaccines exemplified, the specification provides only general guidance with regard to vector design and construction and possible promoters and other regulatory elements that could be used to drive expression of the three genes included in the vaccine. Specific guidance is not provided for achieving expression in appropriate cell types at levels suitable to elicit a protective antibody response.

State of the prior art and predictability of the art. The claims encompass DNA vaccines as well as viral vector vaccines which fall into the realm of gene therapy. However, gene therapy and DNA vaccination are not routinely successful. Therefore, the disclosure must enable the full scope of the claimed vaccine compositions with specific guidance.

At the outset it is noted that the term "vaccine" denotes an intended use for producing a protective or preventive immune response.

As a first issue, the specification fails to provide specific guidance on the parameters for vaccine delivery over the very broad scope of the claims. **Eck et al.** (1996, of record) teaches that numerous factors complicate the gene therapy art (page 81), which have not been shown to be overcome by routine experimentation. These include the following: the fate of the DNA vector itself (volume of distribution, rate of clearance into tissues, etc.), the *in vivo* consequences of altered gene expression and protein function, the fraction of vector taken up by the target cell population, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA produced, the amount and stability of the protein produced, and the protein's compartmentalization within the cell, or its secretory fate, once produced. These factors differ dramatically based on the vector used, the protein being produced, and the disease being treated.

As a second issue, the disclosure of a single embodiment of a well-known tumor cell surface receptor antigen (i.e., Her2/Neu) delivered as a recombinant expression vector in combination with two well-known immune response altering molecules (i.e., 4-1BB ligand and B7-2) into a mouse model prior to tumor formation is insufficient evidence of enablement for any vaccine delivering any cell surface receptor antigen by any route of delivery in combination with any two accessory molecules. No general guidelines existed at the time of filing or at present for the synthesis of recombinant expression constructs for the effective delivery of target antigens for vaccination. Undue experimentation would have been required for one skilled in the art to determine whether or not a selected vaccine composition could elicit or enhance antibody titers specific to any cell surface receptor antigen, particularly at a level that would be protective. Furthermore, undue experimentation would have been required for one skilled in the art to determine whether or not any combination of two IRAMs are co-stimulatory, and further determine which IRAMs work with which cell surface receptor antigen. Thus, the specification fails to enable the full scope of the claimed vaccine.

As a third issue, Applicants' own examples demonstrate the unpredictability in the art of DNA vaccines. The specification provides evidence that one group of mice (Group 4), immunized with component vaccine DNA constructs pLNCX-Rat-Neu + pLNCX-B7.2, did **not** exhibit an increased antibody titer compared to controls and did **not** provide any degree of protection upon disease challenge. In fact, the Group 4 mice exhibited an **increased** tumor growth rate and tumors of increased size as compared to controls (Figure 3). Furthermore, Group 5 mice, immunized with pLNCX-Rat-Neu + pLNCX-4-1BBlig, although exhibiting a slightly increased antibody response as compared to controls, did not exhibit any anti-tumor response, thereby demonstrating that an increased antibody response does not correlate to an anti-tumor response. Therefore, these combinations of DNA vaccine constructs did not function as a vaccine and aptly demonstrates the unpredictability in the art of DNA vaccines which cannot be overcome by routine experimentation.

As a fourth issue, cancer immunotherapy is not routinely successful and the DNA vaccine art is highly unpredictable. Thus, the art of developing DNA vaccines for cancer immunotherapy is also highly unpredictable. For example, with regard to DNA vaccines, **Leitner et al.** (2000, Vaccine 18:765-777) teaches that the expression level of the antigen, immunogenicity of the antigen, the strain of mouse being used to test the DNA vaccine and the age of the animals, all contribute to the unpredictable nature of DNA vaccines and the unpredictability inherent to different methods of assessing the efficacy of said DNA vaccines (see Table 1, page 767). Leitner et al. further note that "the efficacy of genetic vaccines in many systems has not proven to be satisfactory" (page 766, column 2) and that "[a]lthough genetic vaccines have been significantly improved, they may not be sufficiently immunogenic for the therapeutic vaccination of patients with infectious diseases or cancer in clinical trials" (abstract). The authors further note that antigens can be modified to make them better immunogens (page 769). While modified antigens fall within the scope of the claimed invention, the specification does not provide specific guidance for improving the immunogenicity of the SRA, using nothing more than routine

experimentation. Although Leitner et al. acknowledge that intramuscular and intradermal DNA vaccination may employ different mechanisms in inducing immune responses, the instant specification provides no specific guidance on which vaccine compositions may be suitable for any given route of administration or which routes of administration would be appropriate for any given vaccine composition. Thus, in addition to testing a huge variety of possible combinations, the skilled artisan would need to test different routes of administration for each combination vaccine, different promoters, different mouse strains at varying ages or primate models, and possibly different modified forms of the antigen. Furthermore, since an antibody response does not necessarily correlate to an anti-tumor response or protective immune response, further experiments would be required to evaluate any possible anti-tumor effect or protective effect of the selected vaccine. As a result of the large number of parameters that affect the success of genetic vaccination, intensive investigation has met with limited success.

The state of the art is such that numerous problems exist in regards to administering a DNA vaccine to humans and large animals. **Babiuk et al.** (2003, Vaccine 21: 649-658) teaches that "[i]t is generally recognized that DNA vaccines are often less effective in large animals than in mice" (abstract). With regard to the use of co-stimulatory strategies in combination with DNA vaccines, the authors note that "[t]he complexity of the biological actions of co-stimulatory molecules and cytokines will require much more testing to design optimal stimulation for DNA vaccines" (page 652, column 2, paragraph 3).

The specification fails to provide specific guidance on routes of administration for the various combination vaccines covered by the broad scope of the claims, particularly with regard to raising a protective antigen-specific antibody response. The specification only teaches the use of intradermal injection for raising an anti-tumor antibody response (page 53, lines 20-21), and beyond that, the specification provides only general guidance with regard to routes of administration that were known in the art for DNA vaccines in general. **McCluskie et al.** (1999, Mol. Med. 5:287-300) teaches that the route of delivery of a DNA vaccine influences immune responses in laboratory animals (abstract)

Specifically, in one study McCluskie et al. only observed antibody responses to injected routes of administration of DNA vaccines and not to non-injected routes of administration of DNA vaccines, such as oral routes, sublingual, inhalation, and vaginal wall, because of variation in transfection efficiency (abstract). Among the injected routes, only 5 of 8 routes produced an antibody response. Furthermore, McCluskie et al. teaches that the strength and nature of immune responses to administration of DNA vaccines varies between species and that it is not clear that results from one species are predictive in another (abstract).

The specification fails to provide specific guidance on the multitude of parameters that affect the effectiveness of DNA vaccines. Given the very large number of possible combinations of the three vaccine components, considered with the different types of vectors, promoters, and other regulatory elements that may be used to control expression of the components, considerable guidance is needed to identify a set of parameters that will produce a protective antigen-specific antibody response. **Finn** (2003, Nature Reviews Immunology 3:630-641) teaches numerous factors that determine the effectiveness of a vaccine, such as choosing the right antigen, choosing the right adjuvant, generating the right type of immune response, and elicitation of long-term memory (pages 630-633). Finn further points out that tumor-induced immunosuppression and immune evasion are additional issues that confound the effectiveness of cancer vaccines (page 634). Thus, given the large number of parameters that may be varied, with no guidelines that are generally applicable to the disparate diseases that may be targeted for treatment, considerable experimentation is required to identify vaccines within the scope of the claims that are capable of producing a protective antibody response.

Another factor affecting the immunogenicity of any DNA vaccine is the nucleotide sequence itself. **Donnelly et al.** (1997, Annual Review of Immunology 15:617-648, of record) teaches that "[c]ertain CpG motifs can be stimulatory or inhibitory, suggesting that the presence or absence of these sequences in DNA vaccines could affect the immunogenicity of the vaccine" (page 638, paragraph 1) and

that "[t]hese observations suggest that the plasmid itself functions as an adjuvant or immunomodulator" (page 638, pargraph 1). The authors go on explicitly point out that "[a]ltering the nucleotide sequence of the vector may affect the immunogenicity of DNA vaccines" (page 638, paragraph 1). However, since some motifs are stimulatory and some inhibitory, the effect will be unpredictable. Thus, there are no clear guidelines for developing DNA vaccines that produce the desired response.

Absent specific guidance for identifying other vaccine compositions that produce the claim-designated response, the skilled artisan would have been required to engage in trial and error experimentation. Such experimentation clearly would rise to the standard of undue experimentation.

The art clearly demonstrates that DNA vaccines produce unpredictable responses and that considerable experimentation is required to produce a desired response. Thus, the prior art shows that intensive investigation has met with limited success.

The specification provides no guidance beyond the single working example on how to select an appropriate combination of elements for eliciting a protective antibody response. Since one of skill in the art would not know **what** to make, the skilled artisan would not know **how** to make vaccine compositions that elicit a protective antibody response. Furthermore, for any given combination of elements, given the high degree of unpredictability inherent to the art of DNA vaccination, one of skill in the art would not know how to use the vaccine composition in a manner suitable to raise a protective antibody response, because not all combinations will lead to a protective antibody response. Given the likelihood for a high number of inoperable embodiments that fall within the scope of the claim, one of skill in the art would not know how to distinguish the operable embodiments from the inoperable embodiments, using only routine experimentation.

The court has recognized that physiological activity is unpredictable. *In re Fisher*, 166 USPQ 18 (CCPA 1970). In cases involving unpredictable factors, such as most chemical reactions and

physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved. *In re Fisher*, 166 USPQ 18 (CCPA 1970).

It is not to be left up to the skilled artisan to figure out how to make the necessary starting materials and then to figure out how to use them to produce the biological effects as recited in the claims. The courts held that the disclosure of an application shall inform those skilled in the art how to use applicant's claimed invention, not how to **find out** how to use it for themselves. *In re Gardner et al.* 166 USPQ 138 (CCPA 1970). This specification only teaches what is intended to be done and how it is intended to work, but does not actually teach how to do that which is intended.

Given the unpredictability in the art of DNA vaccination, gene therapy, and cancer immunotherapy, the limited working examples directed to a single combination of antigen plus a first and second IRAM, the limited guidance in the specification for identifying other combinations that would produce the claimed effect, and the broad scope of the claims, undue experimentation would have been required to make and use the claimed vaccine compositions to produce a protective antibody response over the full scope, which covers a vast array of combinations of the three agents specified in the claims in conjunction with additional elements not specified in the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 5, and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 3, 5, and 7 are indefinite in their recitation of "enhancing" because it is unclear relative to what standard or point of reference the antibody titer is considered to be "enhanced." The term "enhancing" is a relative term which renders the claim indefinite. The term "enhancing" is not defined by

the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Thus, the metes and bounds are not clearly set forth.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 5, and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,348,450 (Tang et al., priority to 8/13/1997).

Although the specification fails to provide an enabling disclosure for the very broad scope of the claims, the prior art discloses discrete embodiments that fall within the scope of the claims, and therefore anticipate the claimed invention.

Tang et al. disclose a vaccine composition comprising an adenoviral vector, as well as a DNA viral vector, including the plasmid form, that encodes an antigen, a co-stimulatory molecule and a cytokine. The specification explicitly contemplates a vaccine encoding human carcinoembryonic antigen (CEA), a co-stimulatory molecule, such as B7-1 or B7-2, and a cytokine, such as GM-CSF. See Claims 1-43, especially Claims 4, 8, and 9. See also Examples 4 and 5. The specification discloses a vaccine comprising three individual vectors, with one encoding human CEA, one encoding B7-1, and one encoding GM-CSF. The specification further discloses a vaccine comprising a single vector encoding an antigen, particularly a tumor-associated antigen, a co-stimulatory molecule, and a cytokine (see Claim 9).

Since the claims are directed to compositions, the intended use of the claimed compositions is given patentable weight when making a determination of patentability under 35 U.S.C. 102 only when it serves to define a structural requirement. In composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. See MPEP 2111.02. In the instant case, the prior art structure has all the features required to perform the intended use recited in the claims.

Thus, the claimed invention is disclosed in the prior art.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3, 5, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Conry et al. (1996, of record).

Although the specification fails to provide an enabling disclosure for the very broad scope of the claims, the prior art renders certain discrete embodiments that fall within the scope of the claims obvious.

Conry et al. (1996) disclose co-delivery of genes encoding B7-1 and human carcinoembryonic antigen (CEA) within separate plasmids or a dual plasmid with two independent expression cassettes (page 68). Intramuscular delivery of the dual expression plasmid produced anti-CEA antibody responses and antitumor effects superior to those generated by plasmid DNA encoding CEA alone (Table 2 and Figure 3). The reference further discloses the co-delivery of a plasmid encoding GM-CSF with the plasmid encoding CEA by gene gun, which resulted in augmentation of the CEA-specific antibody response as compared to delivery of the CEA plasmid alone (pages 69-70 and Table 3). The reference further describes the mechanism by which GM-CSF acts on Langerhans cells present in the epidermis to enhance the APC function of those cells (page 71, column 2, paragraph 3).

GM-CSF qualifies as a T cell agent as set forth in the instant specification and B7-1 qualifies as an accessory cell agent as set forth in the instant specification. CEA qualifies as a cell surface receptor antigen (SRA) as set forth in the instant specification.

Since one of skill in the art would have wanted to optimize the antibody response to the tumor-associated antigen CEA, the skilled artisan would have recognized that combining the advantage achieved using the co-stimulatory molecule B7-1 with the advantage achieved using GM-CSF would optimize the antibody response. Thus, the skilled artisan would have been motivated to deliver the dual plasmid encoding both B7-1 and CEA in combination with the plasmid encoding GM-CSF by gene gun delivery to the skin to achieve an improved antibody response as compared to delivery of a plasmid encoding CEA alone, with the understanding that expression of the co-stimulatory molecule B7-1 and the cytokine GM-CSF would lead to improved APC function and thus an improved antibody response and improved anti-tumor effects. Thus, a composition comprising the dual plasmid encoding both B7-1 and CEA and the plasmid encoding GM-CSF would have been obvious. Furthermore, the skilled artisan would have also recognized that delivery as a single plasmid encoding all three components would also be useful for getting all three components expressed in an antigen-presenting cell (APC). Thus, a single plasmid

encoding all three components would also have been obvious. One of skill in the art would have anticipated a reasonable expectation of success for achieving the claim-designated antibody response because improved antibody responses were already demonstrated for each plasmid on its own (i.e., the dual plasmid and the plasmid encoding GM-CSF) and only standard molecular biology techniques are required to make the requisite plasmids. Thus, the claimed vaccine compositions would have been obvious.

Therefore, the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

No claims are allowable.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on (571) 272-4517. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

/Anne-Marie Falk/
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